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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,349	10/19/2001	Luke V. Schneider	020444-000710US	2257

20350 7590 06/03/2003

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/035,349	Applicant(s) Schneider
	Examiner Arun Chakrabarti	Art Unit 1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 23, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-58* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claims 1, 14, 23, 32, 38, 45, and 48 have been amended and new claims 51-58 have been added.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 2, 4, 7-15, 17-25, 28, 30-33, 36-38, 41-43, 45-46, 48-49, and 51-58 are rejected under 35 U.S.C. 103(a) over Brennan (U.S. Patent 5,174,962) (December 29, 1992) in view of Schimdt et al. (U.S. Patent 6,287,780 B1) (September 11, 2001).

Brennan teaches a method for sequencing a terminal portion of an oligomer (Abstract), comprising:

a) contacting the oligomer with a labeling moiety to covalently attach a label to the terminus of the oligomer and form a labeled oligomer, the labeling moiety comprising at least one element having an atomic number from 17 to 77, with the proviso that the element is other than sulfur or phosphorus (Column 5, line 25 to Column 6, line 42 and Examples 3 and 4 and Scheme B on Column 8, line 65 to Column 9, line 27);

b) fragmenting the labeled oligomer using a mass spectrometric fragmentation method to produce labeled oligomer fragments (Scheme B and Column 7, lines 59-63); and

c) analyzing the labeled oligomer fragments using a mass spectrometric fragmentation method to determine the sequence of at least two terminal residues (Figure 1 and Claim 1).

Brennan teaches a method, wherein the labeling moiety comprises at least one element bromine of atomic number 35 (Examples 3 and 4 and Scheme B on Column 8, line 65 to Column 9, line 27).

Brennan teaches a method, wherein the oligomer is selected from oligonucleotide with at least three or four residues (Abstract and Column 5, line 25 to Column 6, line 42 and Examples 3 and 4 and Scheme B on Column 8, line 65 to Column 9, line 27).

Brennan teaches a method, wherein the labeling moiety comprises the element iodine (Column 4, lines 28-34).

Brennan teaches a method, wherein several oligomers, each labeled with a different number of mass defect elements are mixed prior to the fragmenting or analyzing step (Column 5, lines 46-55).

Brennan teaches a method of separating individual labeled oligomers in the labeled oligomer mixture (Column 5, lines 46-55).

Brennan teaches a method, further comprising a step prior to step (a) of isolating a group of oligomers from a biological sample consisting of healthy and diseased sample (Abstract, last two sentences and Column 1, lines 40-51).

Brennan teaches a method, wherein the separating is conducted by at least one method of capillary electrophoresis of the labeled oligomer mixture (Column 11, lines 1-22 and Figure 1)

Brennan teaches a method, wherein the mass spectrometric method uses ESI-TOF MS (Figure 2).

Brennan teaches a method of differentially labeling the oligomers by differentially labeling exposed residues and unexposed residues in the three-dimensional structure and analyzing them (Schemes B-E).

Brennan inherently teaches a method of contacting a second sample of the oligomer with a labeling moiety having two elements with an atomic number from 17 to 77, with the proviso that the elements are other than sulfur or phosphorus and analyzing the labeled tag by mass spectrometric methods to determine both its mass and the number of elements with an atomic number from 17 to 77, such that the mass and number of elements identifies the chemical processes to which the specific chemical of the library has been exposed and the identity of the chemical from the library (Scheme B).

Brennan does not teach the method, wherein the labeling moiety comprises a mass defect moiety.

Schimdt et al. teach the method, wherein the labeling moiety comprises a mass defect moiety. (Abstract and Column 5, lines 59).

Brennan does not teach the method, of determining the sequence of at least two terminal residues of the labeled oligomer, the sequence determination step comprising identifying a mass spectrum data corresponding to the labeled oligomer fragment or a mass spectrum fragment thereof, wherein the identification step is based at least in part on the mass defect of at least a portion of the labeling moiety.

Schimdt et al. teach the method of determining the sequence of at least two terminal residues of the labeled oligomer, the sequence determination step comprising identifying a mass spectrum data corresponding to the labeled oligomer fragment or a mass spectrum fragment

thereof, wherein the identification step is based at least in part on the mass defect of at least a portion of the labeling moiety (Column 5, lines 59, Examples 1-6 and Claims 33-45).

Brennan does not teach the method, wherein the sequence determination step comprises identifying a mass spectrum peak of a fragment comprising the labeling moiety based on the mass defect of the labeling moiety.

Schimdt et al. teach the method, wherein the sequence determination step comprises identifying a mass spectrum peak of a fragment comprising the labeling moiety based on the mass defect of the labeling moiety (Figures 7-14 and Claims 33-45).

Brennan does not teach the method, wherein at least a portion of the labeling moiety of step(a) is a stable isotope of the labeling moiety of step(b) and which differ by 2-8 or more but 16 or less stable isotope and wherein the stable isotope is selected from C-13.

Schimdt et al. teach the method, wherein at least a portion of the labeling moiety of step(a) is a stable isotope of the labeling moiety of step(b) and which differ by 2-8 or more but 16 or less stable isotope and wherein the stable isotope is selected from C (Example 6).

Brennan does not teach the method further comprising separating (by electrophoresis, chromatography or affinity separation) at least a portion of the mixture of labeled analytes prior to the analysis step (d).

Schimdt et al. teach the method further comprising separating (by electrophoresis, chromatography or affinity separation) at least a portion of the mixture of labeled analytes prior to the analysis step (d) (Example 6 and Claims 33-45).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method of determining the sequence of at least two terminal residues of the labeled oligomer, the sequence determination step comprising identifying a mass spectrum data corresponding to the labeled oligomer fragment or a mass spectrum fragment thereof, wherein the identification step is based at least in part on the mass defect of at least a portion of the labeling moiety of Schimdt et al. in the method of Brennan., since Schimdt et al states, "An advantageous embodiment of this invention where cleavable mass labels are employed is the use of fluorinated mass labels when high-resolution mass analysis of labels is employed after cleavage of mass labels from their nucleic acid (Column 5, lines 34-38)." Schimdt et al provides further motivation as Schimdt et al states, "Since fluorinated molecules are not common in living systems, this means that a fluorinated mass label will be distinguishable in the mass spectrum even in the presence of contaminating peaks due to fragmentation of the nucleic acids or of components from buffers and other reagents. In corporation of a number of units of fluorinated aryl ethers is a simple means of introducing a mass defect into the mass label (Column 5, lines 47-56)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method of determining the sequence of at least two terminal residues of the labeled oligomer, the sequence determination step comprising identifying a mass spectrum data corresponding to the labeled oligomer fragment or a mass spectrum fragment thereof, wherein the identification step is based at least in part on the mass defect of at

least a portion of the labeling moiety of Schimdt et al. in the method of Brennan in order to improve the process for determining polynucleotide sequences and also in order to achieve the express advantages, as noted by Schimdt et al., of an invention which provides mass defect fluorinated mass label distinguishable in the mass spectrum even in the presence of contaminating peaks due to fragmentation of the nucleic acids or of components from buffers and other reagents and which also provides incorporation of a number of units of fluorinated aryl ethers leading to a simple means of introducing a mass defect into the mass label.

4. Claims 3, 5, 6, 16, 27, 34, 44, 47, and 50 are rejected under 35 U.S.C. 103(a) over Brennan (U.S. Patent 5,174,962) (December 29, 1992) in view of Schimdt et al. (U.S. Patent 6,287,780 B1) (September 11, 2001) further in view of Meyer et al. (U.S. Patent 6,359,111 B1) (March 19, 2002).

Brennan in view of Schimdt et al. teach the method of claims 1, 2, 4, 7-15, 17-25, 28, 30-33, 36-38, 41-43, 45-46, 48-49, and 51-58 as described above..

Brennan in view of Schimdt et al. do not teach the method, wherein the labeling moiety comprises at least one element yttrium of atomic number 39 to 58.

Meyer et al. teach the method, wherein the labeling moiety comprises at least one element yttrium of atomic number 39 to 58 (Column 22, lines 28-31).

Brennan in view of Schimdt et al. do not teach the method, wherein the labeling moiety comprises europium.

Meyer et al. teach the method, wherein the labeling moiety comprises europium (Column 21, lines 41-50).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein the labeling moiety comprises europium and yttrium of Meyer et al. in the method of Brennan in view of Schimdt et al., since Meyer et al states, "For in vitro diagnostic purposes, fluorescent metal species such as Terbium and Europium may be preferred since their complexes would be chemically similar to In and Y complexes but would be detectable by their fluorescence (Column 21, lines 46-50)." Meyer et al provides further motivation as Meyer et al states, "Preferred radionuclides for use in conjunction with a therapeutic kit are Re, Y, Cu, Rh, Au and Bi (Column 22, lines 28-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein the labeling moiety comprises europium and yttrium of Meyer et al. in the method of Brennan in view of Schimdt et al. in order to improve the process for determining polynucleotide sequences and also in order to achieve the express advantages, as noted by Meyer et al., of an invention which provides preferred metals such as Europium and Yttrium which are detectable by their fluorescence.

5. Claims 26, 29, 35, 39 and 40 are rejected under 35 U.S.C. 103(a) over Brennan (U.S. Patent 5,174,962) (December 29, 1992) in view of Schimdt et al. (U.S. Patent 6,287,780 B1) (September 11, 2001) further in view of Chait et al. (U.S. Patent 6,391,649 B1) (May 21, 2002).

Brennan in view of Schimdt et al. teach the method of claims 1, 2, 4, 7-15, 17-25, 28, 30-33, 36-38, 41-43, 45-46, 48-49, and 51-58 as described above..

Brennan in view of Schimdt et al. do not teach the method, wherein the oligomer is a protein comprising a portion of the tyrosine residue and lipid.

Chait et al. teach the method, wherein the oligomer is a protein comprising a portion of the tyrosine residue and lipid (Abstract, Examples 1 and 2, SEQ ID NO: 1 and Column 20, lines 6-19 and Claim 1).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein the oligomer is a protein and lipid of Chait et al. in the method of Brennan in view of Schimdt et al., since Chait et al states, "The method is applicable to the components of any type of biological matter which are ionizable and may therefore be analyzed by mass spectrometry (Abstract, last sentence)." Chait et al provides further motivation as Chait et al states, "Such analyses may be useful in clinical investigation and diagnosis (Column 20, lines 59-60)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein the oligomer is a protein and lipid of Chait et al. in the method of Brennan in view of Schimdt et al., in order to improve the process for determining structure and composition of protein and lipid and also in order to achieve the express advantages, as noted by Chait et al., of an invention which is applicable to the components of any type of biological matter which are ionizable and may

therefore be analyzed by mass spectrometry and which is useful in clinical investigation and diagnosis.

Response to Amendment

6. In response to amendment, 112 (second paragraph) rejection and previous 102(b) and 103(a) rejections have been withdrawn. However, new 103(a) rejections have been included.

Response to Arguments

7. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to

37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

May 26, 2003

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